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| HOFFMANN & BARON, LLP 6900 JERICHO TURNPIKE SYOSSET, NY 11791 | | | EXAMINER HIBBERT, CATHERINE S | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/539,476

Applicant(s)

SOSA ET AL.

Examiner

Catherine S. Hibbert

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-72 is/are pending in the application.
- 4a) Of the above claim(s) 2, 7-21, 24, 28, 30-54, 56 and 58-72 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-6, 22, 23, 25-27, 29, 55 and 57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 June 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsman's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 9/19/2005
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

This is the First Action on the Merits of US Application No. 10/539,476, filed 20 June 2005, which claims priority to PCT/CU2003/000018, filed 19 December 2003, which claims foreign priority to Cuban Application No. CU 202-0337, filed 27 December 2002. Claims 1-72 are pending. Claims 2, 7-21, 24, 28, 30-54, 56 and 58-72 are withdrawn. Claims 1, 3-6, 22-23, 25-27, 29, 55 and 57 are under examination in this action.

Election/Restrictions

Applicant's election without traverse of Group I (i.e., claims 1-31, 55, and 57) and of the following species:

- 5' transcription regulation element: "homologous to a DNA sequence that naturally enhances and/or regulates gene expression in plant cells" (claim 3);
- the element from rice (claim 4);
- the sequence corresponding to SEQ. ID NO: 10 (claim 6);
- the first exon described in claim 23; the second exon described in claim 27;
- the exon/intron/exon region described in SEQ. ID NO:6 (claim 26); and
- the DNA vector "for the expression of DNA sequences in plant cells containing an artificial promoter responding to claim 1" (claim 57).

in the reply filed on 10 April 2008 is acknowledged. Applicants indicate that Claims 1, 3-6, 22-23, 25-27, 29, 55 and 57 are readable on the elected species.

Claims 2, 7-21, 24, 28, 30-54, 56 and 58-72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions/species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10 April 2008.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

Applicants claim to foreign priority to Cuban Application No. CU 202-0337, filed 27 December 2002, is acknowledged but it is noted that Applicant cannot rely upon the foreign priority papers to overcome a prior art rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Information Disclosure Statement

The information disclosure statement filed 19 September 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein that has been lined through has not been considered because the documents were missing.

Specification

The disclosure is objected to because of the following informalities: 35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is replete with terms which are not clear, concise and exact. The specification should be revised carefully in order to comply with 35 U.S.C. 112, first paragraph. Examples of some unclear, inexact or verbose terms used in the specification are the following phrases: "importat" (page 1, line 18); "multiples efforts" (page 1, line 19); "However, with the exception of the RNA secondary structure of all these viral leaders is not complex, is not determined another common element between its nucleotide sequences responding for its translational enhancer properties" (page 3, lines 13-16); and "the GC content of the sequence from the TATA box to the transcription initiation site must not necessarily to be high" (page 5, lines 5-7).

A substitute specification in proper idiomatic English and in compliance with 37 CFR 1.52(a) and (b) is required. The substitute specification filed must be accompanied by a statement that it contains no new matter.

Claim Objections

Claims 3 and 22 are objected to because of the following informalities:

Claim 3 is missing a strike-through line for "char" in line 1.

Claim 22 has an inappropriate comma between the word "fused" and the period at the end of the sentence.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 22, 25-26, 29, 55 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding Claims 6, 26 and 29, the term "corresponds to" is a relative term which renders the claims indefinite. The term "corresponds to" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, regarding Claim 6, it is unclear whether the phrase "corresponds to SEQ ID NO:10" requires 100% sequence identity to SEQ ID NO:10 or whether the Claim encompasses analogous but not identical sequences to SEQ ID NO:10. Therefore, one of ordinary skill in the art would not be able to determine the meets and bounds of Applicants invention.

Claim 22 recites the limitation "the 5' transcription regulation region" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim because Claim 1, from which Claim 22 depends, refers to a 5' transcription regulation element, but does not refer to a regulation "region".

Claim 25 recites the limitation "the CTCC motif and/or its homologous sequences CTC, TCC and TC" in lines 2-3. There is insufficient antecedent basis for this limitation

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in the claim because Claim 1, from which Claim 25 depends, does not refer to CTCC motifs.

Regarding Claim 55 and 57, the term: "an artificial promoter responding to claim 1". The use of the term "responding to" in the context of the claim is unclear because it is unclear what is meant by a promoter responding to a claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 3-6, 23, 26, 55 and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by McElroy et al in "Isolation of an Efficient Actin Promoter for Use in Rice Transformation" (The Plant Cell, February 1990, Vol. 2, page 163-171).

Claim 1 is drawn to an artificial promoter characterized for being a recombinant DNA molecule promoting expression in plant cells of a DNA sequence fused to its 3'

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end, comprising: a) a 5' transcription regulator element followed by, b) an artificial core promoter comprising a TATA box, a nucleotide sequence with a GC content lower than 64% and a transcription initiation site fused in its 3' end to, c) a synthetic nucleotide sequence "transcriptable but not translatable", conformed by a first chimerical Exon, an artificial Intron able to enhance the expression of genes fused to it in plant cells, and a second chimerical Exon with translation enhancement properties of a gene inserted downstream. Claims 55 and 57 are drawn to a cassette and vector for the expression of DNA sequences in plant cells containing an artificial promoter "responding" to claim 1 and to a DNA vector for plant cell transformation comprising said expression cassette, respectively. Although it is noted that the phrase "responding to" in Claims 55 and 57 renders the claims indefinite (see above), in the interest of compact prosecution, the term "responding to Claim 1" will be examined under the meaning "according to Claim 1".

McElroy et al teach a recombinant promoter that promotes the expression of the bacterial β -glucuronidase gene in plant (rice) cells contained within an expression cassette carried in a vector (p. 169, ¶ 3-5), wherein the recombinant promoter includes a 5'- transcription regulation element from the rice actin-1 gene followed by a core promoter comprising a TATA box, a nucleotide sequence with a GC content lower than 64% (e.g. p. 168, ¶ 2, lines 1-3) and a transcription initiation site fused in its 3' end to a nucleotide sequence containing a first Exon, an Intron able to enhance the expression of genes fused to it in rice cells, and a second Exon that enhances translation of the inserted GUS gene (e.g. abstract, lines 8-9), which meets the limitations of the instant

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Claims 1, 3-4 and 55 and 57 (see especially p. 164, ¶¶ 3-4 and Figure 1 and legend; p.165, Figure 2 and legend; and p. 166, Figure 3 and legend). McElroy et al teach that the 5' transcription regulation element comprises the region from -43 to -310 of the rice actin-1 gene transcription initiation site and corresponds to a fragment of SEQ ID NO:10, which meets the limitations of instant Claims 5-6 (see especially p.165, Figure 2 and legend).

Additionally, McElroy teaches wherein the region of the recombinant non-coding first Exon comprises motifs C and A rich and wherein the nucleotide sequence of the first non-coding Exon/"enhancer" intron/second Exon "region" corresponds to a fragment of SEQ ID NO:6. For example, McElroy et al recite: "The 79-bp noncoding exon located 3' of the putative Act1 TATA box is GC-rich (77.5%) and consists of a number of tandemly repeated A/TCC triplets (p. 164, ¶ 4, lines 6-9), which meets the limitations of Claim 23 and 26.

Therefore, McElroy et al anticipates Claims 1, 3-6, 23, 26 and 55 and 57.

Claims 1, 3-6, 23, 25-27, 29, 55 and 57 are rejected under 35 U.S.C. 102(b) and 102(e) as being anticipated by McElroy et al in "Rice Actin Gene and Promoter" (US Patent 5,641,876, issued 24 June 1997, entire document).

Claims 1, 3-6, 23, 26, 55 and 57 are as described above. In addition, Claim 25 is drawn to an artificial promoter according to claim 1, which Intron from the artificial Exon/Intron/Exon region comprises sequences wherein the CTCC motif and/or its

homologous sequences CTC, TCC and TC are frequently repeated. Furthermore, Claim 27 is drawn to an artificial promoter according to claim 1 wherein the second Exon from the artificial Exon/Intron/Exon region comprises sequence motifs with high C and A content, and Claim 29 specifies within Claim 27 that the nucleotide sequence of the second Exon from the artificial Exon/Intron/Exon region corresponds to SEQ ID NO: 1.

Regarding Claims 1, 3-6 and 55-57, McElroy et al (US 5,641,876) teach an invention that describes a recombinant promoter functional in an expression cassette contained within a vector for plant cell transformation (see abstract and Claims 1-4). Specifically, McElroy et al teach that said recombinant promoter comprises a core promoter region comprising a TATA box, "a nucleotide sequence" with a GC content lower than 64%, and a transcription initiation site fused in its 3' end to a nucleotide sequence containing a first Exon, an Intron, and second Exon. For example, McElroy et al report that:

a 2.1 kbp 5' of the Act1 gene's translation initiation codon, containing 1.3 kb of 5' untranscribed sequence, the 5' transcribed but untranslated exon, 5'-intron and part of the first coding exon of the rice Act1 gene, is capable of conferring high level expression of foreign gene in transformed rice material. Thus this region can be used to activate the constitutive expression of foreign genes in transgenic plants of rice and other agronomically important plants; the 5'-intron of the rice Act1 gene can stimulate the expression of a foreign gene in transformed rice material [thus this (and the other introns of the rice Act1 gene) will be able to increase the expression of foreign genes in transformed plants of rice (and

other agronomically important plants) when cloned into such genes] (see column 20, lines 8-22).

Regarding Claims 23 and 26, McElroy et al teach wherein the region of the recombinant non-coding first Exon comprises motifs C and A rich and wherein the nucleotide sequence of the non-coding Exon/Intron/second Exon region corresponds to a fragment of SEQ ID NO:6. For example, McElroy et al report that a 79-bp noncoding exon located 3' of the Act1 TATA box is GC-rich and consists of a number of tandemly repeated A/TCC triplets (e.g. see column 14, lines 35-38).

Regarding Claims 25, 27 and 29, McElroy et al teach the sequence of the Intron within the Exon/Intron/Exon region, showing sequences wherein the CTC, TCC and TC motifs are frequently repeated (e.g. see column 5-6, SEQ ID NO:4, bp position around 1697-2010), and showing wherein the nucleotide sequence of the second Exon from the Exon/Intron/Exon region comprises sequence motifs with high C and A content and corresponds to SEQ ID NO: 1 (e.g. see column 5-6, SEQ ID NO:4, starting at bp position 2044).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over McElroy *et al.* (US 5,641,876), as applied to claim 1 above, and further in view of McElroy *et al.* in "Construction of expression vectors based on the rice actin 1 (ACT1) 5' region for use in monocot transformation", (Mol Gen Genet, December, 1991, Vol. 231, No. 1, pages 150-160). Claim 22 is drawn to an artificial promoter according to claim 1 wherein the 5' transcription regulation region comprises 2 or more regulator elements from different origins operatively fused.

McElroy *et al.* (US 5,641,876) teaches the promoter of Claim 1 (described above).

However, McElroy *et al.* (US 5,641,876) differs from the invention claimed in the instant claim 22 in that while it teaches recombinant promoters containing various sequences of the Act1 5' regulatory regions, McElroy *et al.* (US 5,641,876) fails to teach wherein the 5' transcription regulation region comprises 2 or more regulatory elements from different origin operatively fused.

McElroy *et al.* (Mol Gen Genet) teach rice Act-1-GUS promoters with a 5' transcription regulation region comprising rice and CaMV 35S regulatory elements operatively fused.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have utilized the chimeric promoter sequences of McElroy *et al.* (Mol Gen Genet) in the promoter constructs taught in McElroy *et al.* (US 5,641,876) because McElroy *et al.* teach that various chimeric promoter elements were available and were routinely and successfully used for constructing and characterizing plant promoters (e.g. p.150, abstract).

One would have been motivated at the time the invention was made to have utilized chimeric 5' regulatory sequences such as the CaMV 35S regulatory sequences of McElroy *et al.* (Mol Gen Genet), in the construct of McElroy *et al.* (US 5,641,876) because the McElroy recite "By utilizing both the *Act1* intron I and optimized *Gus* translation initiation site, a 40-fold stimulation in G-us expression from the CaMV 35S promoter has been achieved in transformed rice cells; very similar results were obtained

in transformed maize cells (see abstract, lines 18-23). In addition, both constructs were from the same field of endeavor (plant promoters) and both are directed to the same problem sought to be solved (more effective plant promoters).

Absent evidence to the contrary, one would have a reasonable expectation of success combining the teachings of the art because the use of the CaMV 35S regulatory sequences for the purpose of constructing plant chimeric promoters was routinely practiced at the time the teachings of McElroy *et al.* (Mol Gen Genet), and McElroy *et al.* (US 5,641,876) were published.

In view of the foregoing, the promoter of claims 1 and 22, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC §103(a).

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Catherine S. Hibbert, Ph.D., whose telephone number is (571)270-3053. The examiner can normally be reached on M-F 8AM-5PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D., can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully submitted,

Catherine S. Hibbert
Examiner/AU1636

/David Guzo/
Primary Examiner
Art Unit 1636